G. Gabel
436892

```
=> fil reg

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                                                         ENTRY    SESSION
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=> e ldl/cn 5

E1            1     LDK 1003/CN
E2            1     LDK-TR/CN
E3            0 --> LDL/CN
E4            1     LDL 500/CN
E5            1     LDL RECEPTOR (HUMAN GENE OLR1 REDUCED)/CN

=> e vldl/cn 5

E1            1     VLCE2/CN
E2            1     VLCFA CONDENSING ENZYME (ARABIDOPSIS THALIANA GENE CUT1)/CN
E3            0 --> VLDL/CN
E4            1     VLDL RECEPTOR (CATTLE NON-O-GLYCOSYLATED
ENDOTHELIUM-SPECIFI
                    C ISOFORM)/CN
E5            1     VLDL RECEPTOR (HUMAN ISOFORM II FRAGMENT)/CN

=> s (ldl ? or vldl ?)/cn

             12 LDL ?/CN
              4 VLDL ?/CN
L1           16 (LDL ? OR VLDL ?)/CN

=> e "apob-100"/cn 5

E1            1     APOATROPINE, NITRO-, NITRATE/CN
E2            1     APOATROPINE, TETRACHLOROAURATE(1-)/CN
E3            0 --> APOB-100/CN
E4            1     APOBASINOSIDE/CN
E5            1     APOBAYIN, 4-O-METHYL-, PENTAACETATE/CN

=> e apolipoprotein/cn
```

```
E1            1      APOLIPOPHORIN-III (DEROBRACHUS GEMINATUS FAT BODY
PRECURSOR
                     C-TERMINAL FRAGMENT)/CN
E2            1      APOLIPOPOPROTEINASE (STREPTOCOCCUS PYOGENES STRAIN D734
GENE
                      SOF22)/CN
E3            0 --> APOLIPOPROTEIN/CN
E4            1      APOLIPOPROTEIN (CORYNEBACTERIUM MATRUCHOTII STRAIN
ATCC-1426
                     6 CALCIUM-PRECIPITATING 5.0-KILODALTON)/CN
E5            1      APOLIPOPROTEIN (CORYNEBACTERIUM MATRUCHOTII STRAIN
ATCC-1426
                     6 CALCIUM-PRECIPITATING 5.5-KILODALTON)/CN
E6            1      APOLIPOPROTEIN (HUMAN GENE APOC4)/CN
E7            1      APOLIPOPROTEIN A-1/CN
E8            1      APOLIPOPROTEIN A-1 (BEIJING DUCK BLOOD)/CN
E9            1      APOLIPOPROTEIN A-1 (PSI-P700) (OENOTHERA ELATA
PLASTID-ENCOD
                     ED GENE PSAA)/CN
E10           1      APOLIPOPROTEIN A-1 (SPARUS AURATA LIVER)/CN
E11           1      APOLIPOPROTEIN A-I/CN
E12           1      APOLIPOPROTEIN A-I (ANAS STRAIN BEIJING-DUCK LIVER)/CN

=> e apolipoprotein b 100/cn

E1            1      APOLIPOPROTEIN B (MONODELPHIS DOMESTICA C-TERMINAL
FRAGMENT)
                     , RNA-EDITED/CN
E2            1      APOLIPOPROTEIN B (SALMON C-TERMINAL FRAGMENT REDUCED)/CN
E3            0 --> APOLIPOPROTEIN B 100/CN
E4            1      APOLIPOPROTEIN B MRNA CYTIDYLATE DEAMINASE/CN
E5            1      APOLIPOPROTEIN B MRNA EDITING ENZYME/CN
E6            1      APOLIPOPROTEIN B MRNA EDITING PROTEIN (HUMAN)/CN
E7            1      APOLIPOPROTEIN B MRNA-EDITING PROTEIN (HUMAN)/CN
E8            1      APOLIPOPROTEIN B RECEPTOR (HUMAN CLONE PCR631 FRAGMENT)/CN
E9            1      APOLIPOPROTEIN B RECEPTOR (HUMAN MONOCYTE-MACROPHAGE)/CN
E10           1      APOLIPOPROTEIN B RNA EDITING DEAMINASE (HUMAN CLONE
.LAMBDA.
                     NI.1.0/.LAMBDA.NI2.2 CATALYTIC SUBUNIT REDUCED)/CN
E11           1      APOLIPOPROTEIN B-100 (HUMAN PRECURSOR)/CN
E12           1      APOLIPOPROTEIN B48 RECEPTOR (HUMAN PLACENTA GENE APOB48R
ISO
                     FORM 2)/CN

=> s e11

L2            1 "APOLIPOPROTEIN B-100 (HUMAN PRECURSOR)"/CN

=> fil medl,caplus,biosis,embase,wpids,jicst

COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              16.67      16.82

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=> s (l1 or l2 or ldl or vldl or (low or very low)(w)density(a)lipoprotein!
or (d10.516.532.515 or d12.776.521.550)/ct or lipoprotein!(a)(ldl or vldl))

L3       34777 FILE MEDLINE
L4       22781 FILE CAPLUS
L5       27401 FILE BIOSIS
L6       24922 FILE EMBASE
L7         904 FILE WPIDS
L8        6302 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L9      117087 (L1 OR L2 OR LDL OR VLDL OR (LOW OR VERY LOW)(W) DENSITY(A)
               LIPOPROTEIN! OR (D10.516.532.515 OR D12.776.521.550)/CT OR
LIPOP
               ROTEIN!(A)(LDL OR VLDL))

=> s (l1 or ldl or vldl or (low or very low)(w)density(a)lipoprotein! or
(d10.516.532.515 or d12.776.521.550)/ct or lipoprotein!(a)(ldl or vldl))

L10      34777 FILE MEDLINE
L11      22780 FILE CAPLUS
L12      27401 FILE BIOSIS
L13      24922 FILE EMBASE
L14        904 FILE WPIDS
L15       6302 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L16     117086 (L1 OR LDL OR VLDL OR (LOW OR VERY LOW)(W) DENSITY(A)
LIPOPROTEI
               N! OR (D10.516.532.515 OR D12.776.521.550)/CT OR
LIPOPROTEIN!(A)
               (LDL OR VLDL))

=> s l16 and (l2 or apo b100 or apolipoprotein b 100 or d12.776.70.400.300/ct
or abetalipoproteinenia)

L17       3135 FILE MEDLINE
L18        650 FILE CAPLUS
L19        544 FILE BIOSIS
```

```
L20         474 FILE EMBASE
L21           7 FILE WPIDS
L22          20 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L23        4830 L16 AND (L2 OR APO B100 OR APOLIPOPROTEIN B 100 OR
D12.776.70.40
                0.300/CT OR ABETALIPOPROTEINENIA)

=> s l23 and (elisa or enzyme link? immunosorbent assay or
(e5.478.567.380.360 or e1.450.495.410.350.200 or e1.450.495.410.380.200 or
e5.478.567.350.170 or e5.478.588.400.170)/ct)

L24         103 FILE MEDLINE
L25          22 FILE CAPLUS
L26          13 FILE BIOSIS
L27          12 FILE EMBASE
L28           1 FILE WPIDS
L29           2 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L30         153 L23 AND (ELISA OR ENZYME LINK? IMMUNOSORBENT ASSAY OR
(E5.478.56
                7.380.360 OR E1.450.495.410.350.200 OR E1.450.495.410.380.200
                OR E5.478.567.350.170 OR E5.478.588.400.170)/CT)

=> s l23 and (?electrophoresis? or (e5.196.401 or h1.181.529.307.437 or
h1.181.278.414(/ct or sandwich)

MISSING OPERATOR '81.278.414(/CT'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l23 and (?electrophoresis? or (e5.196.401 or h1.181.529.307.437 or
h1.181.278.414)/ct or sandwich)

L31         353 FILE MEDLINE
L32          49 FILE CAPLUS
L33          57 FILE BIOSIS
L34          58 FILE EMBASE
L35           0 FILE WPIDS
LEFT TRUNCATION IGNORED FOR '?ELECTROPHORESIS?' FOR FILE 'JICST-EPLUS'
L36           7 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L37         524 L23 AND (?ELECTROPHORESIS? OR (E5.196.401 OR
H1.181.529.307.437
                OR H1.181.278.414)/CT OR SANDWICH)
Left truncation is not valid in the specified search field in the
specified file.  The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you
used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
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Implied proximity is used in search fields indexed as single words, for example, the Basic Index.

=> s (l37 or l30) and (clear? or releas? or remov? or excret?) and (structure or conformat? or gene)

L38 10 FILE MEDLINE
L39 2 FILE CAPLUS
L40 6 FILE BIOSIS
L41 6 FILE EMBASE
L42 0 FILE WPIDS
L43 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L44 24 (L37 OR L30) AND (CLEAR? OR RELEAS? OR REMOV? OR EXCRET?) AND (STRUCTURE OR CONFORMAT? OR GENE)

=> s l44 and (low? or decreas?) and cholesterol

L45 4 FILE MEDLINE
L46 1 FILE CAPLUS
L47 1 FILE BIOSIS
L48 2 FILE EMBASE
L49 0 FILE WPIDS
L50 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L51 8 L44 AND (LOW? OR DECREAS?) AND CHOLESTEROL

=> dup rem l51

PROCESSING COMPLETED FOR L51
L52 7 DUP REM L51 (1 DUPLICATE REMOVED)

=> d cbib abs 1-7;s l44 not l51

L52 ANSWER 1 OF 7 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
1998227207 EMBASE Acrolein is a product of lipid peroxidation reaction: Formation of free acrolein and its conjugate with lysine residues in oxidized **low density lipoproteins**. Uchida K.; Kanematsu M.; Morimitsu Y.; Osawa T.; Noguchi N.; Niki E.. K. Uchida, Laboratory of Food and Biodynamics, Nagoya University, Graduate Sch. of Bioagric. Sciences, Nagoya 464-8601, Japan. uchidak@nuagr1.agr.nagoya-u.ac.jp. Journal of Biological Chemistry 273/26 (16058-16066) 26 Jun 1998.
Refs: 35.
ISSN: 0021-9258. CODEN: JBCHA3. Pub. Country: United States. Language: English. Summary Language: English.
AB Lipoprotein peroxidation, especially the modification of **apolipoprotein B-100**, has been implicated to play an important role in the pathogenesis of atherosclerosis. However, there have been few detailed insights into the chemical mechanism of derivatization of apolipoproteins during oxidation. In the present study, we provide evidence that the formation of the toxic pollutant acrolein (CH2=CH-CHO) and its conjugate with lysine residues is involved in the

oxidative modification of human **low** density lipoprotein (**LDL**). Upon incubation with **LDL**, acrolein preferentially reacted with lysine residues. To determine the **structure** of acrolein-lysine adduct in protein, the reaction of acrolein with a lysine derivative was carried out. Employing N(.alpha.)-acetyllysine, we detected a single product, which was identified to be a novel acrolein-lysine adduct, N(.alpha.)-acetyl-N(.epsilon.)-(3-formyl-3,4-dehydropiperidino)lysine. The acid hydrolysis of the adduct led to the derivative that was detectable with amino acid analysis. It was revealed that, upon in vitro incubation of **LDL** with acrolein, the lysine residues that had disappeared were partially recovered by N(.epsilon.)-(3-formyl-3,4- dehydropiperidino)lysine. In addition, we found that the same derivative was detected in the oxidatively modified **LDL** with Cu2+ and that the adduct formation was correlated with **LDL** peroxidation assessed by the consumption of .alpha.-tocopherol and cholesteryl ester and the concomitant formation of cholesteryl ester hydroperoxide. **Enzyme-linked immunosorbent assay** that measures free acrolein revealed that a considerable amount of acrolein was **released** from the Cu2+-oxidized **LDL**. Furthermore, metal-catalyzed oxidation of arachidonate was associated with the formation of acrolein, indicating that polyunsaturated fatty acids including arachidonate represent potential sources of acrolein generated during the peroxidation of **LDL**. These results indicate that acrolein is not just a pollutant but also a lipid peroxidation product that could be ubiquitously generated in biological systems.

L52 ANSWER 2 OF 7 MEDLINE

97248593 Document Number: 97248593. Folding of the amino-terminal domain of apolipoprotein B initiates microsomal triglyceride transfer protein-dependent lipid transfer to nascent very **low** density lipoprotein. Ingram M F; Shelness G S. (Department of Comparative Medicine, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina 27157-1040, USA.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Apr 11) 272 (15) 10279-86. Journal code: HIV. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The initial assembly of apolipoprotein B100 (apoB) into lipoprotein particles occurs cotranslationally. To examine steps required to initiate this process, the intracellular folding and assembly of the amino-terminal 28% of apoB (apoB28) was examined using several criteria including nonreducing gel **electrophoresis**, sensitivity to dithiothreitol (DTT)-mediated reduction, and buoyant density gradient centrifugation. In hepatoma cells, after a 1-min pulse with radiolabeled amino acids, labeled apoB28 migrated during gel **electrophoresis** in the folded position and was resistant to reduction in vivo with 2 mM DTT. A similar rate and extent of folding was observed in Chinese hamster ovary cells, a microsomal triglyceride transfer protein (MTP)-negative cell line that can neither lipidate nor efficiently secrete apoB28. Amino-terminal folding of apoB28 was essential for its subsequent intracellular lipidation as apoB28

synthesized in hepatoma cells under reducing conditions remained lipid poor (d > 1.25 g/ml) and was retained intracellularly. Upon DTT **removal**, reduced apoB28 underwent a process of rapid (t1/2 approximately 2 min) post-translational folding followed by a slower process of MTP-dependent lipidation. As with the cotranslational assembly pathway, post-translational lipidation of apoB28 displayed a strict dependence upon amino-terminal folding. We conclude that: 1) folding of the amino-terminal disulfide bonded domain of apoB is achieved prior to the completion of translation and is independent of MTP and events associated with buoyant lipoprotein formation and 2) domain-specific folding of apoBs amino-terminal region is required to initiate MTP-dependent lipid transfer to nascent apoB in the hepatic endoplasmic reticulum.

L52 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2001 BIOSIS
1996:189727 Document No.: PREV199698745856. Reversal of hypercholesterolemia in **low** density lipoprotein receptor knockout mice by adenovirus-mediated **gene** transfer of the very **low** density lipoprotein receptor. Kobayashi, Kunihisa; Oka, Kazuhiro; Forte, Trudy; Ishida, Brian; Teng, Babie; Ishimura-Oka, Kazumi; Nakamuta, Makoto; Chan, Lawrence (1). (1) Dep. Cell Biol. Med., Baylor Coll. Med., Houston, TX 77030 USA. Journal of Biological Chemistry, (1996) Vol. 271, No. 12, pp. 6852-6860. ISSN: 0021-9258. Language: English.

AB We have used the technique of adenovirus-mediated **gene** transfer to study the in vivo function of the very **low** density lipoprotein receptor (VLDLR) in **low** density lipoprotein receptor (LDLR) knockout mice. We generated a replication-defective adenovirus (AdmVLDLR) containing mouse VLDLR cDNA driven by a cytomegalovirus promoter. Transduction of cultured Hepa (mouse hepatoma) cells and LDLR-deficient CHO-ldlA7 cells in vitro by the virus led to high-level expression of immunoreactive VLDLR proteins with molecular sizes of 143 kDa and 161 kDa. Digestion of the cell extract with the enzymes neuraminidase, N-glycanase, and O-glycanase resulted in the stepwise **lowering** of the apparent size of the 161-kDa species toward the 143-kDa species. LDLR (-/-) mice fed a 0.2% **cholesterol** diet were treated with a single intravenous injection of 3 times 10-9 plaque-forming units of AdmVLDLR. Control LDLR (-/-) mice received either phosphate-buffered saline or AdLacZ, a similar adenovirus containing the LacZ cDNA instead of mVLDLR cDNA. Comparison of the plasma lipids in the 3 groups of mice indicates that in the AdmVLDL animals, total **cholesterol** is reduced by apprx 50% at days 4 and 9 and returned toward control values on day 21. In these animals, there was also a apprx 30% reduction in plasma apolipoprotein (apo) E accompanied by a 90% fall in apoB-100 on day 4 of treatment. By FPLC analysis, the major reduction in plasma **cholesterol** in the AdmVLDLR animals was accounted for by a marked reduction in the intermediate density lipoprotein/**low** density lipoprotein (IDL/**LDL**) fraction. Plasma **VLDL**, IDL/**LDL**, and HDL were isolated from the three groups of animals by ultracentrifugal flotation. In the AdmVLDLR animals, there was substantial loss (apprx 65%) of protein and **cholesterol** mainly in the IDL/**LDL** fraction on days 4 and 9. Nondenaturing gradient gel **electrophoresis** indicates a preferential loss of the IDL peak although the **LDL** peak was also reduced. When 125I-IDL was administered intravenously into animals on day 4, the AdmVLDLR animals

cleared the 125I-IDL at a rate 5-10 times higher than the AdLacZ animals. We conclude that adenovirus-mediated transfer of the VLDLR **gene** induces high-level hepatic expression of the VLDLR and results in a reversal of the hypercholesterolemia in 0.2% **cholesterol** diet-fed LDLR (-/-, mice. The VLDLR overexpression appears to greatly enhance the ability of these animals to **clear** IDL, resulting in a marked **lowering** of the plasma IDL/ **LDL**. Further testing of the use of the VLDLR **gene** as a therapeutic **gene** for the treatment of hypercholesterolemia is warranted.

L52 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2001 ACS
1996:517244 Document No. 125:186815 Clinically applicable mutation screening
in familial hypercholesterolemia. Nissen, Henrik; Guldberg, Per; Hansen, Annebirthe Bo; Petersen, Niels Erik; Hoerder, Mogens (Department Clinical Chemistry, Odense University Hospital, Odense, 5000, Den.). Hum. Mutat., 8(2), 168-177 (English) 1996. CODEN: HUMUE3. ISSN: 1059-7794.
AB Mutations in the **LDL** receptor (LDLR) **gene** and the codon 3500 region of the apolipoprotein (apo) B-100 **gene** result in the clin. indistinguishable phenotypes designated familial hypercholesterolemia (FH) and familial defective apo B-100 (FDB), resp. Introduction of genetic diagnosis in phenotypic FH families may **remove** the diagnostic inaccuracies known from traditional clin./biochem. FH diagnosis and allow more differentiated prognostic evaluations and genetic counseling of FH/FDB families. Previous genetic screening methods for FH have, however, been too cumbersome for routine use, however. To overcome these problems, we designed a mutation screening assay based on the highly sensitive denaturing gradient gel **electrophoresis** (DGGE) technique. The setup allows within 24 h to pinpoint if and where a potential mutation is located in the LDLR promoter, the 18 LDLR **gene** exons and corresponding intronic splice site sequences, or in the codon 3500 region of apo B-100. The pinpointed region is subsequently sequenced. As an evaluation of the sensitivity, we demonstrated the ability of the assay to detect 27 different mutations or polymorphisms covering all the examd. regions, except LDLR exon 16. In conclusion, a simple, but sensitive, clin. applicable mutation screening assay based on the DGGE principle may reveal
the underlying mutation in most FH/FDB families and offer a tool for a more differentiated prognostic and therapeutic evaluation in FH/FDB.

L52 ANSWER 5 OF 7 MEDLINE
95094432 Document Number: 95094432. Detection of familial defective **apolipoprotein B-100** among patients clinically diagnosed with heterozygous familial hypercholesterolemia in maritime Canada. Morash B; Guernsey D L; Tan M H; Dempsey G; Nassar B A. (Department of Physiology and Biophysics, Dalhousie University, Halifax, Nova Scotia, Canada.) CLINICAL BIOCHEMISTRY, (1994 Aug) 27 (4) 265-72. Journal code: DBV. ISSN: 0009-9120. Pub. country: United States.
Language:
English.
AB Familial defective **apolipoprotein B-100** (FDB) is a genetic disorder resulting from a mutation in the **apolipoprotein B-100** (apo B-100) **gene**, most frequently at position 3500, in which arginine is substituted for

glutamine in the mature protein. This mutation drastically **decreases** the affinity of the mutant apo B-100 particle for the **low**-density lipoprotein (**LDL**) receptor, and hence **decreases** the **clearance** of **cholesterol** from the circulation. Familial hypercholesterolemia (FH), also a disorder of lipid metabolism, results from mutations in the **gene** for the **LDL** receptor. Both FDB and heterozygous FH occur at approximately the same frequency (1 in 500) among Caucasians and both produce clinical symptoms and signs that can be indistinguishable. Polymerase chain reaction (PCR) amplification and subsequent restriction analysis have been used to detect the substitution at codon 3500 in the apo B-100 **gene** using mutagenic PCR primers. At least one proband from 10 unrelated families with a history of hypercholesterolemia was screened by mutagenic PCR for FDB. Only one of 10 patients demonstrated the mutation for FDB. The mutant apo B-100 allele was shown to segregate with other clinically affected family members. These results demonstrate that molecular analysis is essential to distinguish between FDB and heterozygous FH in hypercholesterolemic families.

L52 ANSWER 6 OF 7 MEDLINE DUPLICATE 1

94014801 Document Number: 94014801. Human very **low** density lipoprotein **structure**: interaction of the C apolipoproteins with **apolipoprotein B-100**. Yang C Y; Gu Z W; Valentinova N; Pownall H J; Lee B; Yang M; Xie Y H; Guyton J R; Vlasik T N; Fruchart J C; et al. (Department of Medicine, Baylor College of Medicine, Houston, TX 77030..) JOURNAL OF LIPID RESEARCH, (1993 Aug) 34 (8) 1311-21. Journal code: IX3. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB **Very low density lipoproteins** (**VLDL**) are a heterogenous population of particles differing in size and composition. Heparin-Sepharose chromatography yields three **VLDL** subfractions. Two subfractions, VLDLNR-1 and VLDLNR-2, which are not retained by heparin, contain little or no detectable apolipoprotein (apo)E. According to negative stain electron microscopy, VLDLNR-1 is slightly larger than VLDLNR-2. The third fraction, VLDLR, is composed of smaller particles that are retained by the heparin-Sepharose and contain apoE. The C apolipoproteins of the respective **VLDL** subfractions transfer to 1-palmitoyl-2-oleoyl phosphatidylcholine (POPC) single bilayer vesicles giving three subfractions designated VLDLNR-1-C, VLDLNR-2-C, and VLDLR-C. The protein, phospholipid, and **cholesterol** (free + esterified) contents **decrease** in the order VLDLR > VLDLNR-2 > VLDLNR-1. Triglyceride content **decreases** in the opposite order. POPC treatment of each **VLDL** subfraction increases the phospholipid and **decreases** the protein, triglyceride, and cholesteryl ester contents, while free **cholesterol** remains unchanged. According to immunological analysis of each subfraction with well-characterized monoclonal antibodies, the accessibility of some epitopes of apoB-100 on **VLDL** is changed by POPC treatment. Electron-microscopic analysis of POPC-treated **VLDL** subfraction reveals vacancies on the surfaces of each particle. VLDLNR-1, VLDLNR-2, and VLDLR are resistant to thrombin cleavage, whereas the lipoproteins lacking C apolipoproteins are not. Thrombin cleavage (8 h) of apoB-100 of VLDLNR-2-C and VLDLR-C gives two fragments, T1 and T2, that are converted to smaller fragments only after prolonged treatment. In

contrast, apoB-100 of VLDLNR-1-C is converted into small fragments after 8
h thrombin treatment. These results suggest that **removal** of apoCs affects the accessibility and **conformation** of apoB-100 in the individual **VLDL** subfractions in the region near residue 3249, which is the primary thrombin cleavage site and the epitope of monoclonal antibody 4C11.

L52 ANSWER 7 OF 7 MEDLINE
90257509 Document Number: 90257509. Genetic heterogeneity of plasma lipoproteins in the mouse: control of **low** density lipoprotein particle sizes by genetic factors. Jiao S; Cole T G; Kitchens R T; Pfleger B; Schonfeld G. (Department of Internal Medicine, Washington University School of Medicine, St. Louis, MO 63110..) JOURNAL OF LIPID RESEARCH, (1990 Mar) 31 (3) 467-77. Journal code: IX3. ISSN: 0022-2275. Pub. country: United States. Language: English.

AB In order to assess the genetic control of sizes and concentrations of mouse plasma **low** density (**LDL**) and high density lipoproteins (HDL), we used gel permeation fast protein liquid chromatography (FPLC) and nondenaturing gradient polyacrylamide gel **electrophoresis** to measure the particle sizes of **LDL** and HDL. Using chromatography we also quantified **LDL-cholesterol** and HDL-**cholesterol** concentrations in plasma and used them as indexes of plasma concentrations of the respective particles among 10 inbred strains (AKR/J, BALB/cByJ, C3H/HeJ, C57BL/6J, C57BL/6ByJ, C57L/J, DBA/1LacJ, 129/J, NZB/BINJ, SWR/J) and three sets of recombinant inbred (RI) strains (AKXL/TyJ, BXH/TyJ, CXB/ByJ) of mice. HDL had a dichotomous distribution among the 10 inbred strains. One group had large HDL particle sizes and high HDL-**cholesterol** concentrations. Another group had smaller HDL particles and **lower** HDL-**cholesterol** concentrations, and HDL sizes and HDL-**cholesterol** concentrations were significantly correlated. In the RI strains, HDL sizes and HDL-**cholesterol cholesterol** concentrations **clearly** segregated with one or another of the progenitor strains, and RI strain distributions showed a strong linkage to
the apolipoprotein (apo) A-II **gene** (Apoa-2). In contrast, **LDL-cholesterol** concentrations and particle sizes on FPLC did not show dichotomous distributions among the 10 inbred strains. In RI strains, the configuration of the **LDL** FPLC profiles and **LDL-cholesterol** concentrations did resemble one or another of the progenitors in the majority of cases, but **LDLs** of several RI strains resembled neither progenitor strain in profile configuration, and **LDL-cholesterol** concentrations were both greater and smaller than those of progenitor strains. However, **LDL** particle diameters (as judged by peaks of **LDL-cholesterol** profiles) did segregate with progenitors in 29/33 (88%) of RI strains suggesting that a major **gene** may affect **LDL** size. In attempting to identify a major **LDL**-size determining **gene**, we compared apoB **gene** restriction fragment length polymorphisms (RFLPs) to the distributions of peak **LDL** sizes in RI strains. Concordance rates of peak **LDL** sizes to apoB **gene** polymorphisms were 18/22 (82%) for the EcoRV RFLP, 5/7 (71%) for HindIII RFLP, and 23/29 (79%) for both (range of P values 0.90-0.95). Thus we could not unequivocally implicate the apoB

gene in determining the size of **LDL** particles. In summary, the genetic control of **LDL** sizes is more complicated than is the case for HDL; however, the differences in **LDL** size among these strains of mice may be controlled by a major, as yet unidentified, **gene**.

L53 6 FILE MEDLINE
L54 1 FILE CAPLUS
L55 5 FILE BIOSIS
L56 4 FILE EMBASE
L57 0 FILE WPIDS
L58 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L59 16 L44 NOT L51

=> dup rem l59

PROCESSING COMPLETED FOR L59
L60 10 DUP REM L59 (6 DUPLICATES REMOVED)

=> d cbib abs 1-10

L60 ANSWER 1 OF 10 MEDLINE
1999456370 Document Number: 99456370. Apolipoprotein B mRNA editing and apolipoprotein **gene** expression in the liver of hyperinsulinemic fatty Zucker rats: relationship to very low density lipoprotein composition. Elam M B; von Wronski M A; Cagen L; Thorngate F; Kumar P; Heimberg M; Wilcox H G. (Veterans Affairs Medical Center, Division of Clinical Pharmacology, University of Tennessee, Memphis 38163, USA.. melam@utmemkl.utmem.edu) . LIPIDS, (1999 Aug) 34 (8) 809-16. Journal code: L73. ISSN: 0024-4201. Pub. country: United States. Language: English.
AB We previously demonstrated increased apolipoprotein B (apoB) mRNA editing, elevated levels of mRNA for the catalytic component of the apoB mRNA editing complex, apobec-1, and increased secretion of the product of the edited mRNA, apoB48, in **very low density lipoproteins** (**VLDL**) in primary cultures of Sprague-Dawley rat hepatocytes following insulin treatment. In order to determine the effect of in vivo hyperinsulinemia on these processes, we determined apoB mRNA editing, apobec-1 expression, hepatic expression of mRNA for apoB and other **VLDL** apoproteins, and the quantity and composition of plasma **VLDL** in the hyperinsulinemic fatty Zucker rat. Total apoB mRNA content of the livers of the fatty rats and lean littermates did not differ; however, edited apoB message coding for hepatic apo B48, and abundance of mRNA for the catalytic subunit of the apoB mRNA editing complex, apobec-1, was increased by 1.7- and 3.3-fold, respectively, in fatty rats. ApoCIII mRNA abundance was increased in livers of fatty rats as well, but the abundance of hepatic apoE mRNA in the fatty animal was not different from that of the lean rat. Hepatic apoAI mRNA abundance was also increased in the fatty rats. Associated with

increased apoB mRNA editing, was the 1.7-fold increase in the fraction of apoB in plasma as apoB48 in fatty rats. **VLDL**-triglyceride and -apoB in plasma were 15- and 3-fold higher, respectively, in fatty Zucker rats compared to lean littermates, indicating both enrichment of **VLDL** with triglycerides and increased accumulation of **VLDL** particles. Increased hepatic expression of mRNA for apoCIII and apoAI was associated with increased content of apoC (and relative depletion of apoE) in **VLDL** of fatty rats, and plasma apoAI was increased in fatty Zucker rats, primarily in the HDL fraction. The current study provides further evidence that chronic exposure to high levels of insulin influences both the quantity of and lipid/apoprotein composition of **VLDL** in plasma. The increased apoC and decreased apoE (as well as increased triglyceride) content of **VLDL** in the fatty Zucker rat observed in the current study may affect **VLDL clearance** and therefore may be a factor in the observed accumulation of **VLDL** in the plasma of the fatty hyperinsulinemic Zucker rats.

L60 ANSWER 2 OF 10 MEDLINE DUPLICATE 1

1998298110 Document Number: 98298110. Acrolein is a product of lipid peroxidation reaction. Formation of free acrolein and its conjugate with lysine residues in oxidized **low density lipoproteins**. Uchida K; Kanematsu M; Morimitsu Y; Osawa T; Noguchi N; Niki E. (Laboratory of Food and Biodynamics, Nagoya University Graduate School of Bioagricultural Sciences, Nagoya 464-8601, Japan.. uchidak@nuagr1.agr.nagoya-u.ac.jp) . JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Jun 26) 273 (26) 16058-66. Journal code: HIV. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Lipoprotein peroxidation, especially the modification of **apolipoprotein B-100**, has been implicated to play an important role in the pathogenesis of atherosclerosis. However, there have been few detailed insights into the chemical mechanism of derivatization of apolipoproteins during oxidation. In the present study, we provide evidence that the formation of the toxic pollutant acrolein (CH2=CH-CHO) and its conjugate with lysine residues is involved in the oxidative modification of human low density lipoprotein (**LDL**). Upon incubation with **LDL**, acrolein preferentially reacted with lysine residues. To determine the **structure** of acrolein-lysine adduct in protein, the reaction of acrolein with a lysine derivative was carried out. Employing Nalpha-acetyllysine, we detected a single product, which was identified to be a novel acrolein-lysine adduct, Nalpha-acetyl-Nepsilon-(3-formyl-3,4-dehydropiperidino)lysine. The acid hydrolysis of the adduct led to the derivative that was detectable with amino acid analysis. It was revealed that, upon in vitro incubation of **LDL** with acrolein, the lysine residues that had disappeared were partially recovered by Nepsilon-(3-formyl-3, 4-dehydropiperidino)lysine. In addition, we found that the same derivative was detected in the oxidatively modified **LDL** with Cu2+ and that the adduct formation was correlated with **LDL** peroxidation assessed by the consumption of alpha-tocopherol and cholesteryl ester and the concomitant formation of cholesteryl ester hydroperoxide. **Enzyme-linked immunosorbent assay** that measures free acrolein revealed that a considerable amount of acrolein was **released** from the

Cu2+-oxidized **LDL**. Furthermore, metal-catalyzed oxidation of arachidonate was associated with the formation of acrolein, indicating that polyunsaturated fatty acids including arachidonate represent potential sources of acrolein generated during the peroxidation of **LDL**. These results indicate that acrolein is not just a pollutant but also a lipid peroxidation product that could be ubiquitously generated in biological systems.

L60 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2001 BIOSIS
1999:42191 Document No.: PREV199900042191. Evaluation of an immunoseparation method for quantitative measurement of remnant-like particle-cholesterol in serum and plasma. Leary, Elizabeth Teng (1); Wang, Tao; Baker, Daniel J.; Cilla, Donald D.; Zhong, Jianhua; Warnick, G. Russell; Nakajima, Katsuyuki; Havel, Richard J.. (1) Pacific Biometrics Inc., 220 West Harrison St., Seattle, WA 98119 USA. Clinical Chemistry, (Dec., 1998) Vol. 44, No. 12, pp. 2490-2498. ISSN: 0009-9147. Language: English.

AB Substantial evidence indicates that triglyceride-rich lipoprotein remnants are atherogenic. Additional research has, however, been limited by available methods for separation and quantification of remnants. We have evaluated an immunoseparation assay developed to measure cholesterol in remnant-like particles (RLP-C). This method uses monoclonal antibodies to human **apolipoproteins B-100** and A-1 to **remove** most of the **apolipoprotein B-100**-containing lipoproteins (namely **LDL** and nascent **VLDL**) and apolipoprotein A-1-containing lipoproteins (namely chylomicrons and HDL), leaving behind a fraction of triglyceride-rich lipoproteins, including chylomicron and **VLDL** remnants, both of which are enriched in apolipoprotein E. Cholesterol in the unbound fraction is measured with a sensitive enzymatic assay. The RLP-C concentration was highly correlated with total triglyceride-rich lipoproteins (sum of **VLDL**-cholesterol and IDL-cholesterol) separated by ultracentrifugation and by polyacrylamide gel **electrophoresis** (r = 0.86 and 0.76, respectively). The within-run and run-to-run imprecision (CV) of the assay was -6% and 10%, respectively. The assay was not affected by hemoglobin up to 5000 mg/L (500 mg/dL), bilirubin up to 342 mmol/L (20 mg/dL), glucose up to 67 mmol/L (1200 mg/dL), or ascorbic acid up to 170 mmol/L (3.0 mg/dL). In 726 subjects (men, n = 364; women, n = 362) in the US, the 75th percentiles of RLP-C concentration were 0.17 mmol/L (6.6 mg/dL) and 0.23 mmol/L (8.8 mg/dL) in sera obtained after overnight fasting or randomly, respectively. A group of 151 patients from nine US centers and one Canadian center with coronary artery atherosclerosis established by angiography had higher median RLP-C concentrations than 302 gender- and age-matched controls ($P < 0.05$). We conclude that the RLP-C assay compares favorably to ultracentrifugation and **electrophoresis** and provides a convenient and economical approach to measure triglyceride-rich lipoprotein remnants in routine clinical laboratories.

L60 ANSWER 4 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
1998029362 EMBASE Denaturing gradient gel electrophoretic analysis of codons

3456-3553 of the apolipoprotein-B **gene** in 106 type 11a hyperlipoproteinaemic individuals. Nissen H.; Day L.B.; Horder M.; Humphries S.E.; Day I.N.M.. Dr. I.N.M. Day, Univ. Dept. of Clinical Boichemistry, Level D South Laboratory Block, Southampton General Hospital, Southampton, United Kingdom. Annals of Clinical Biochemistry 35/1 (137-139) 1998.
Refs: 6.
ISSN: 0004-5632. CODEN: ACBOBU. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Familial defective **apolipoprotein B-100** (FDB) is commonly attributable to mutation of glutamine to arginine in codon 3500 of the apolipoprotein B (APOB) **gene**. APOB, the protein component of low-density lipoprotein (**LDL**) acts as the ligand for the **LDL** receptor (LDLR), mediating the **clearance** of **LDL** from plasma. This mutation causes hypercholesterolaemia and consequent coronary artery disease phenotypically similar to familial hypercholesterolaemia (FH) attributable to LDLR **gene** defects. APOB **gene** mutation R3500Q is prevalent in Western Europe, attributable to a single founder mutation, and occurring at up to one in 1000 in the general population and 1%-2% in apparent FH collections. Many studies applying direct assay of patient groups for R3500Q have been undertaken, but there are indications that other ligand defects exist, R3531C and R3500W having been described. Different regions or countries may display different mutational spectra which can be instructive for research and useful for establishing genetic diagnostic assays. Codon region 3456-3553 of the APOB **gene** contains the mutations so far identified, and therefore is a strong candidate for a functional role in receptor binding. We have applied denaturing gradient gel **electrophoresis** (DGGE), a sensitive de novo mutation scanning technique, to this region in 106 apparent FH index cases from the South of England.

L60 ANSWER 5 OF 10 MEDLINE DUPLICATE 2

1998394729 Document Number: 98394729. Mutation screening of the LDLR **gene** and ApoB **gene** in patients with a phenotype of familial hypercholesterolemia and normal values in a functional **LDL** receptor/apolipoprotein B assay. Nissen H; Lestavel S; Hansen T S; Luc G; Bruckert E; Clavey V. (Department of Clinical Chemistry, Odense University Hospital, Denmark.. Nissen@gamma.dou.dk) . CLINICAL GENETICS, (1998 Jul) 54 (1) 79-82. Journal code: DDT. ISSN: 0009-9163. Pub. country: Denmark. Language: English.

AB Mutations in the **LDL** receptor (LDLR) or the **apolipoprotein B-100 genes** causing familial hypercholesterolemia (FH) and familial defective **apolipoprotein B-100** (FDB), two of the most frequent inherited diseases, are the underlying genetic defects in a small proportion of patients suffering from premature atherosclerotic heart disease. Consequently, secure diagnostic tools for these conditions allowing early preventive measures are needed. Since clinical and biochemical diagnosis often is inaccurate, assays analyzing patient LDLR function and **LDL** affinity have been established. These assays are, however, not able **clearly** to differentiate between suspected FH/FDB samples and normal controls. To evaluate if this may be caused by other hitherto undescribed genetic defects or to failure of the

functional assays, we undertook denaturing gradient gel **electrophoresis** based mutation screening of the LDLR **gene** and the codon 3456 3553 region of the apolipoprotein B **gene** in six French FH/FDB patients with normal outcomes on functional assays. In all six patients, pathogenic LDLR mutations were found, including three previously undescribed mutations, suggesting that failure of the functional assays explains the normal results found in some phenotypic FH/FDB patients and illustrating the need for DNA based screening techniques for routine genetic diagnosis in FH/FDB.

L60 ANSWER 6 OF 10 BIOSIS COPYRIGHT 2001 BIOSIS
1996:438014 Document No.: PREV199699151620. Clinically applicable mutation screening in familial hypercholesterolemia. Nissen, Henrik (1); Guldberg, Per; Hansen, Annebirthe Bo; Petersen, Niels Erik; Horder, Mogens. (1) Dep.
Clin. Chem., Odense Univ. Hosp., 5000 Odense C Denmark. Human Mutation, (1996) Vol. 8, No. 2, pp. 168-177. ISSN: 1059-7794. Language: English.
AB Mutations in the **LDL** receptor (LDLR) **gene** and the codon 3500 region of the apolipoprotein (apo) B-100 **gene** result in the clinically indistinguishable phenotypes designated familial hypercholesterolemia (FH) and familial defective apo B-100 (FDB), respectively. Introduction of genetic diagnosis in phenotypic FH families may **remove** the diagnostic inaccuracies known from traditional clinical/biochemical FH diagnosis and allow more differentiated prognostic evaluations and genetic counseling of FH/FDB families. Previous genetic screening methods for FH have, however, been too cumbersome for routine use, however. To overcome these problems, we designed a mutation screening assay based on the highly sensitive denaturing gradient gel **electrophoresis** (DGGE) technique. The setup allows within 24 hr to pinpoint if and where a potential mutation is located in the LDLR promoter, the 18 LDLR **gene** exons and corresponding intronic splice site sequences, or in the codon 3500 region of apo B-100. The pinpointed region is subsequently sequenced. As an evaluation of the sensitivity, we demonstrated the ability of the assay to detect 27 different mutations or polymorphisms covering all the examined regions, except LDLR exon 16. In conclusion, a simple, but sensitive, clinically applicable mutation screening assay based on the DGGE principle may reveal the underlying mutation in most FH/FDB families and offer a tool for a more differentiated prognostic and therapeutic evaluation in FH/FDB.

L60 ANSWER 7 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
92051417 EMBASE Document No.: 1992051417. Increased **removal** of .beta.-**very low density lipoproteins** after ethinyl estradiol is associated with increased mRNA levels for hepatic lipase, lipoprotein lipase, and the low density lipoprotein receptor in Watanabe heritable hyperlipidemic rabbits. Demacker P.N.M.; Staels B.; Stalenhoef A.F.H.; Auwerx J.. General Internal Medicine Div., Department of Medicine, University Hospital Nijmegen, Geert Grooteplein Zuid 8,6500 HB Nijmegen, Netherlands. Arteriosclerosis and Thrombosis 11/6 (1652-1659) 1991.
ISSN: 1049-8834. CODEN: ARTTE5. Pub. Country: United States. Language: English. Summary Language: English.
AB The mechanism by which ethinyl estradiol (EE) decreases the concentration

of lipids in the d<1.019 g/ml fraction (.beta.-very low density lipoprotein [.beta.- **VLDL**]) of homozygous Watanabe heritable hyperlipidemic (WHHL) rabbits was studied. Treatment with EE increased the activity of hepatic lipase (HL) twofold to threefold in postheparin plasma and in liver biopsies. Postheparin plasma and adipose tissue lipoprotein lipase (LPL) activities were also increased twofold to fourfold after EE. The effects of EE on HL and LPL activities were associated with a threefold to sixfold elevation in liver HL mRNA and a fourfold elevation in adipose tissue LPL mRNA steady-state levels, pointing to an effect of EE on HL and LPL **gene** transcription. EE also increased liver low density lipoprotein (**LDL**) receptor mRNA levels threefold to fivefold. These results suggest a concerted action of LPL, HL, and the **LDL** receptor in the **removal** of .beta.-**VLDL** in homozygous WHHL rabbits with a defective **LDL** receptor. In addition, the content of apolipoprotein E in the d<1.019 g/ml fraction changed toward normal after EE. Because the remaining particles contained **apolipoprotein B-100** almost exclusively, it is likely that apolipoprotein E-containing .beta.-**VLDLs** are preferentially **removed**. This may be the result of the increased activity of LPL and HL influencing the **conformation** of apolipoprotein E on the .beta.-**VLDL** particle in such a way that it is directly **removed** from the circulation, possibly by the induced **LDL** receptor.

L60 ANSWER 8 OF 10 MEDLINE DUPLICATE 3
86270021 Document Number: 86270021. Interaction of tryptic peptides of **apolipoprotein B-100** with dimyristoylphosphatidylcholine. Cardin A D; Jackson R L. BIOCHIMICA ET BIOPHYSICA ACTA, (1986 Jul 18) 877 (3) 366-71. Journal code: A0W. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB **Apolipoprotein B-100**, the major protein constituent of human plasma **low-density lipoproteins** (**LDL**), was carboxyamidomethylated, digested with trypsin and the water-soluble tryptic peptides were coincubated with liposomes of dimyristoylphosphatidylcholine (DMPC). At 24.3 degrees C the peptides induced lipid solubilization as evidenced by optical **clearing** of the lipid-peptide mixture. Lipid-peptide complexes were isolated by density-gradient ultracentrifugation in KBr and had the following properties: DMPC/peptide ratio of 5.6 (w/w); buoyant density of 1.07-1.09 g/ml; discoidal morphology (51 +/- 4 X 260 +/- 28 A) as determined by electron microscopy; and molecular weight of 1.5 X 10(6) as determined by nondenaturing polyacrylamide gel **electrophoresis**. Compared to liposomes and sonicated vesicles of DMPC, the lipid-peptide complexes had a more rigid **structure** as assessed by fluorescence polarization. Whereas intact **LDL** had 42% alpha-helix and 15% beta-pleated sheet, the lipid-peptide complexes contained 70% alpha-helix and less than 5% beta-pleated sheet. The lipid-peptide complexes did not bind to the fibroblast high-affinity **LDL** receptor. These results show that specific regions in **apolipoprotein B-100** which interact with phospholipid have an amphipathic character and may represent primary sites for lipid-protein interaction in **LDL**.

L60 ANSWER 9 OF 10 MEDLINE

86004714 Document Number: 86004714. High-mannose **structure** of apolipoprotein-B from **low-density lipoproteins** of human plasma. Vauhkonen M; Viitala J; Parkkinen J; Rauvala H. EUROPEAN JOURNAL OF BIOCHEMISTRY, (1985 Oct 1) 152 (1) 43-50. Journal code: EMZ. ISSN: 0014-2956. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.

AB Human plasma **low-density lipoproteins** were purified by flotation followed by gel filtration. The protein moiety of the lipoproteins, apolipoprotein-B, which was detected by polyacrylamide gel **electrophoresis** as the only protein component, contained 4.4% (by weight) carbohydrate. Glycopeptides liberated from apolipoprotein-B by pronase were fractionated by affinity chromatography on concanavalin-A--Sepharose. The results indicated that high-mannose glycopeptides interacting strongly with the lectin comprise about 37% of the total monosaccharides of apolipoprotein-B. Thus, as compared to the total serum glycoproteins having about 5% of their monosaccharides in high-mannose glycopeptides, **low-density lipoproteins** are relatively enriched in these **structures** amounting up to about 10% of the total high-mannose oligosaccharides in serum. The rest of the carbohydrates in **low-density lipoproteins** are suggested to be mainly biantennary acidic oligosaccharides interacting weakly with concanavalin A. The oligomannosidic chains from native **low-density lipoproteins** and isolated glycopeptides were **released** by digestion with endo-beta-N-acetylglucosaminidase H. Thin-layer chromatography of the **released** oligosaccharides indicated that apolipoprotein-B contains five different oligomannosidic **structures** varying in the number of the mannose residues from Man5GlcNAc to Man9GlcNAc. Separation of the per-O-benzoylated high-mannose oligosaccharides by high-pressure liquid chromatography revealed the same polymeric **structures** in a molar ratio (from Man5 to Man9) of 10:2:3:2:3. Apolipoprotein-B in **low-density lipoproteins** was calculated to contain five high-mannose chains in total. The different high-mannose oligosaccharides liberated by endo-beta-N-acetylglucosaminidase H were isolated with high-pressure liquid chromatography after reduction with NaBH4, and subjected to methylation analysis with gas-liquid chromatography--mass spectrometry. The data of these studies and the results of exoglycosidase treatment suggest the following **structure** for the main high-mannose oligosaccharide: (formula: see text) The higher polymeric **structures** are composed of chains in which the Man5GlcNAc **structure** is continued by one to four Man(alpha 1-2) residues.

L60 ANSWER 10 OF 10 MEDLINE

85097041 Document Number: 85097041. Apolipoprotein B: **removal** of lipids by sodium cholate and reassociation of a lipid-free apoprotein with dipalmitoyl phosphatidylcholine. Akimova E I; Melgunov V I. BIOCHEMISTRY INTERNATIONAL, (1984 Oct) 9 (4) 463-73. Journal code: 9Y9. ISSN: 0158-5231. Pub. country: Australia. Language: English.

AB Apolipoprotein B (apoB) of human plasma low-density lipoprotein has been solubilized with sodium cholate added in an amount highly above its critical micellar concentration. During isolation by gel exclusion chromatography on Sepharose CL-4B, the apoB forms mixed micelles of protein and detergent that are free of endogenous lipids. The circular

dichroic spectra of the sodium cholate-solubilized apoB indicate significant heterogeneity within the fractions obtained by gel chromatography. The peak position fraction of apoB taken from the column was used for reassociation with dipalmitoyl phosphatidylcholine (DPPC). A soluble apoB-DPPC complex has been prepared by incubation of apoB-sodium cholate and DPPC-sodium cholate solutions at 42 degrees C, followed with detergent **removal** by extensive dialysis in the presence of a XAD-2 ion-exchange resin. Data from negative-stain electron microscopy suggests the incorporation of solubilized apoB into single-bilayer phospholipid vesicles. Upon reassociation with phospholipid, a shift (to shorter wavelengths) occurs in the intrinsic fluorescence of the apoB, thus indicating a transfer of tryptophan residues to a more hydrophobic environment. Sodium dodecylsulfate-polyacrylamide **electrophoresis** gives a single band (apparent Mr 370,000) for apoB after solubilization, purification and interaction with the phospholipid.

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'IN' IS NOT A VALID FIELD CODE
L61          40 FILE MEDLINE
L62          58 FILE CAPLUS
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L64          41 FILE EMBASE
L65          16 FILE WPIDS
L66           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
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L72         114 FILE WPIDS
L73          75 FILE JICST-EPLUS

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L80           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
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L82 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
2000:335659 Document No. 132:343330 Methods and compositions to lower plasma
cholesterol levels. **Medford, Russell M.**; Saxena, Uday (Atherogenics, Inc., USA). PCT Int. Appl. WO 2000028332 A1 20000518, 50 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US26519 19991109. PRIORITY: US 1998-PV107644 19981109.

AB A method for detg. whether a compd. binds to a lipoprotein, e.g. LDL or VLDL, in a manner which will lower plasma cholesterol is provided that includes assessing the ability of the compd. to form a complex with the lipoprotein, e.g., LDL or VLDL, and then detg. whether the newly formed complex causes a change in the structure of apoB-100 that results in increased binding affinity to the LDL receptor. Also disclosed is a method for lowering cholesterol in a host in need thereof, including a human, that includes the administration of an effective amt. of a compd. which binds to cholesterol-carrying lipoprotein (e.g. LDL or VLDL) in a manner that alters the three dimensional configuration of the lipoprotein and increases the binding affinity of the apoB-100 protein to the LDL receptor, including those on the surface of a hepatic cell.

L82 ANSWER 2 OF 8 MEDLINE DUPLICATE 2
2000233733 Document Number: 20233733. Decreased secretion of ApoB follows inhibition of ApoB-MTP binding by a novel antagonist. Bakillah A; Nayak N;
Saxena U; Medford R M; Hussain M M. (Department of Pathology, School of Medicine, MCP Hahnemann University, Philadelphia, Pennsylvania 19129, USA.) BIOCHEMISTRY, (2000 Apr 25) 39 (16) 4892-9. Journal code: A0G. ISSN: 0006-2960. Pub. country: United States.
Language:
English.

AB Apolipoprotein B (apoB) and microsomal triglyceride transfer protein (MTP)
are essential for the efficient assembly of triglyceride-rich lipoproteins. Evidence has been presented for physical interactions between these proteins. To study the importance of apoB-MTP binding in apoB secretion, we have identified a compound, AGI-S17, that inhibited (60-70% at 40 microM) the binding of various apoB peptides to MTP but not to an anti-apoB monoclonal antibody, 1D1, whose epitope overlaps with an MTP binding site in apoB. AGI-S17 had no significant effect on the lipid transfer activity of the purified MTP. In contrast, another antagonist, BMS-200150, did not affect apoB-MTP binding but inhibited MTP's lipid

transfer activity. The differential effects of these inhibitors suggest two functionally independent, apoB binding and lipid transfer, domains in MTP. AGI-S17 was then used to study its effect on the lipid transfer and apoB binding activities of MTP in HepG2 cells. AGI-S17 had no effect on cellular lipid transfer activities, but it inhibited coimmunoprecipitation of apoB with MTP. These studies indicate that AGI-S17 inhibits apoB-MTP binding but has no effect on MTP's lipid transfer activity. Experiments were then performed to study the effect of inhibition of apoB-MTP binding on apoB secretion in HepG2 cells. AGI-S17 (40 microM) did not affect cell protein levels but decreased the total mass of apoB secreted by 70-85%. Similarly, AGI-S17 inhibited the secretion of nascent apoB by 60-80%, but did not affect albumin secretion. These studies indicate that AGI-S17 decreases apoB secretion most likely by inhibiting apoB-MTP interactions. Thus, the binding of MTP to apoB may be important for the assembly and secretion of apoB-containing lipoproteins and can be a potential target for the development of lipid-lowering drugs. It is proposed that the apoB binding may represent MTP's chaperone activity that assists in the transfer from the membrane to the lumen of the endoplasmic reticulum and in the net lipidation of nascent apoB, and may be essential for lipoprotein assembly and secretion.

L82 ANSWER 3 OF 8 MEDLINE DUPLICATE 3
2000457946 Document Number: 20387238. Dithiocarbamates: effects on lipid hydroperoxides and vascular inflammatory gene expression. Somers P K; **Medford R M; Saxena U.** (AtheroGenics, Inc., Alpharetta, GA,. USA.pksomers@home.com) . FREE RADICAL BIOLOGY AND MEDICINE, (2000 May 15) 28 (10) 1532-7. Journal code: FRE. ISSN: 0891-5849. Pub. country: United States. Language: English.

AB Dithiocarbamates are a well-defined family of antioxidants that may have therapeutic uses such as in treatment of inflammation and atherosclerosis.

A critical event in the pathogenesis of atherosclerosis is the infiltration of inflammatory cells into the vessel wall. Vascular cell adhesion molecule-1 (VCAM-1) plays a pivotal role in this process by mediating leukocyte binding to endothelial cells. VCAM-1 expression is stimulated by oxidized polyunsaturated fatty acids such as 13-hydroperoxy-octadecadienoic acid (13-HPODE), and this lipid hydroperoxide has been proposed to be a second messenger for induction of VCAM-1 gene expression. Pyrrolidine dithiocarbamate (PDTC) markedly represses cytokine-induced VCAM-1 gene expression in cultured human endothelial cells; however, its effects on the oxidative second messenger pathway are unknown. Using a lipoxygenase (LO) inhibition assay in tandem with a colorimetric assay for lipid peroxides, we determined that PDTC does not inhibit the enzymatic oxidation of linoleic acid to 13-HPODE by LO, but directly interacts with and chemically reduces 13-HPODE. We hypothesize that dithiocarbamates may intercept the oxidative second-messenger-induced expression of VCAM-1 and other redox-regulated genes important in inflammation and atherosclerosis.

L82 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4
2000:452007 Vascular adhesion molecule-1 (VCAM-1), an inflammatory gene target for new therapeutics. **Saxena, Uday; Medford, Russell M.** (Reddy US Inc, Norcross, GA, 30071, USA). Curr. Opin. Cardiovasc., Pulm.

Renal Invest. Drugs, 2(3), 258-262 (English) 2000. CODEN: CCPRFX. ISSN: 1464-8482. Publisher: PharmaPress Ltd..
AB A review with 22 refs. is presented regarding the vascular adhesion mol.-1
(VCAM-1). VCAM-1 appears to be a rational target for controlling monocyte
infiltration obsd. during atherogenesis. It is an attractive approach also because it can complement existing interventions such as lipid lowering. A variety of preclin. approaches have been used to block VCAM-1
activity and some approaches have demonstrated efficacy in animal models.

L82 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2001 BIOSIS
2000:82799 Document No.: PREV200000082799. Lipid modification of 15-lipoxygenase induces inflammatory activity. Lewisch, Sandra A. (1); Suen, Ki-Ling (1); **Medford, Russell M. (1)**; **Saxena, Uday (1)**. (1) AtheroGenics, Inc., Norcross, GA USA. Free Radical Biology & Medicine, (1999) Vol. 27, No. SUPPL. 1, pp. S53. Meeting Info.: 6th Annual
Meeting of the Oxygen Society New Orleans, Louisiana, USA November 18-22, 1999 The Oxygen Society. ISSN: 0891-5849. Language: English.

L82 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2001 BIOSIS
2000:24777 Document No.: PREV200000024777. Fatty acid modification of 15-lipoxygenase confers inflammatory activity. Suen, Ki-Ling (1); Parthasarathy, Sampath; **Medford, Russell M.**; **Saxena, Uday**. (1) AtheroGenics, Inc, Alpharetta, GA USA. Circulation, (Nov. 2, 1999) Vol. 110, No. 18 SUPPL., pp. I.409. Meeting Info.: 72nd Scientific Sessions of the American Heart Association Atlanta, Georgia, USA November 7-10, 1999 ISSN: 0009-7322. Language: English.

L82 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2001 BIOSIS
2000:24200 Document No.: PREV200000024200. Suppression of VCAM-1 and MCP-1 attenuates atherosclerosis in LDL receptor-knockout and ApoE-knockout mouse models. Sundell, Cynthia L. (1); Daugherty, Alan; Stalvey, Angela L.; Hammes, Patricia; Landers, Laura K.; **Medford, Russell M.**; **Saxena, Uday**. (1) AtheroGenics, Inc, Alpharetta, GA USA. Circulation, (Nov. 2, 1999) Vol. 110, No. 18 SUPPL., pp. I.42. Meeting Info.: 72nd Scientific Sessions of the American Heart Association Atlanta,
Georgia, USA November 7-10, 1999 ISSN: 0009-7322. Language: English.

L82 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2001 BIOSIS
1997:3681 Document No.: PREV199799302884. Intracellular oxidant signals regulate the expression of endothelial cell redox-sensitive vascular cell adhesion molecule-1 and monocyte chemoattractant protein-1. **Saxena, Uday (1)**; Alexander, R. W.; Oliff, Lynn K.; Somers, Patricia K.; Parthasarthy, Sampath; **Medford, Russell M.**. (1) AtheroGenics, Inc., Norcross, GA USA. Circulation, (1996) Vol. 94, No. 8 SUPPL., pp. I280-I281. Meeting Info.: 69th Scientific Sessions of the American Heart Association New Orleans, Louisiana, USA November 10-13, 1996 ISSN: 0009-7322. Language: English.

L83 0 FILE MEDLINE

```
L84           1 FILE CAPLUS
L85           0 FILE BIOSIS
L86           0 FILE EMBASE
L87           0 FILE WPIDS
L88           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L89           1 (L67 OR L74) AND (L37 OR L30)

=> d cbib abs


L89  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2001 ACS
2000:335659   Document No. 132:343330  Methods and compositions to lower
plasma
     cholesterol levels.  Medford, Russell M.; Saxena, Uday
     (Atherogenics, Inc., USA).  PCT Int. Appl. WO 2000028332 A1 20000518, 50
     pp.  DESIGNATED STATES: W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY,
     CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR,
     HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
     MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
     SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
     MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES,
     FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG.
     (English).  CODEN: PIXXD2.  APPLICATION: WO 1999-US26519 19991109.
     PRIORITY: US 1998-PV107644 19981109.
AB   A method for detg. whether a compd. binds to a lipoprotein, e.g.
     LDL or VLDL, in a manner which will lower plasma
     cholesterol is provided that includes assessing the ability of the compd.
     to form a complex with the lipoprotein, e.g., LDL or
     VLDL, and then detg. whether the newly formed complex causes a
     change in the structure of apoB-100 that results in increased binding
     affinity to the LDL receptor.  Also disclosed is a method for
     lowering cholesterol in a host in need thereof, including a human, that
     includes the administration of an effective amt. of a compd. which binds
     to cholesterol-carrying lipoprotein (e.g. LDL or VLDL)
     in a manner that alters the three dimensional configuration of the
     lipoprotein and increases the binding affinity of the apoB-100 protein to
     the LDL receptor, including those on the surface of a hepatic
     cell.


=> s l23 and (low? or decreas?) and cholesterol

L90        1680 FILE MEDLINE
L91         287 FILE CAPLUS
L92         222 FILE BIOSIS
L93         207 FILE EMBASE
L94           4 FILE WPIDS
L95          10 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L96        2410 L23 AND (LOW? OR DECREAS?) AND CHOLESTEROL

=> s (three or 3)(w)(d or dimension?) and l96
```

```
L97           4 FILE MEDLINE
L98           2 FILE CAPLUS
L99           2 FILE BIOSIS
L100          2 FILE EMBASE
L101          0 FILE WPIDS
L102          0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L103         10 (THREE OR 3)(W)(D OR DIMENSION?) AND L96

=>

=> s l103 not (181 or 189)

L104          4 FILE MEDLINE
L105          1 FILE CAPLUS
L106          2 FILE BIOSIS
L107          2 FILE EMBASE
L108          0 FILE WPIDS
L109          0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L110          9 L103 NOT (L81 OR L89)

=> dup rem l110

PROCESSING COMPLETED FOR L110
L111           4 DUP REM L110 (5 DUPLICATES REMOVED)

=> d cbib abs 1-4


L111 ANSWER 1 OF 4  MEDLINE                              DUPLICATE 1
1999342033  Document Number: 99342033.   Three-dimensional
     structure of low density lipoproteins by
     electron cryomicroscopy. Orlova E V; Sherman M B; Chiu W; Mowri H; Smith
L
     C; Gotto A M Jr. (Verna and Marrs McLean Department of Biochemistry,
     Baylor College of Medicine, Houston, TX 77030, USA. ) PROCEEDINGS OF THE
     NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Jul
     20) 96 (15) 8420-5.  Journal code: PV3. ISSN: 0027-8424. Pub. country:
     United States. Language: English.
AB   Human low density lipoproteins (LDL
     ) are the major cholesterol carriers in the blood. Elevated
     concentration of LDL is a major risk factor for atherosclerotic
     disease. Purified LDL particles appear heterogeneous in images
     obtained with a 400-kV electron cryomicroscope. Using multivariate
     statistical and cluster analyses, an ensemble of randomly oriented
     particle images has been subdivided into homogeneous subpopulations, and
     the largest subset was used for three-dimensional
     reconstruction. In contrast to the general belief that below the lipid
     phase-transition temperature (30 degrees C) LDL are
     quasi-spherical microemulsion particles with a radially layered
core-shell
     organization, our three-dimensional map shows that
     LDL have a well-defined and stable organization. Particles consist
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of a higher-density outer shell and **lower**-density inner lamellae-like layers that divide the core into compartments. The outer shell consists of **apolipoprotein B-100**, phospholipids, and some free **cholesterol**.

L111 ANSWER 2 OF 4 MEDLINE

96237803 Document Number: 96237803. Fenofibrate reduces plasma cholesteryl ester transfer from HDL to **VLDL** and normalizes the atherogenic, dense **LDL** profile in combined hyperlipidemia. Guerin M; Bruckert E; Dolphin P J; Turpin G; Chapman M J. (Institut National de la Sante et de la Recherche Medicale (INSERM), Unite 321, Pavillon Benjamin Delessert, Hopital de la Pitie, Paris, France.) ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (1996 Jun) 16 (6) 763-72. Journal code: B89. ISSN: 1079-5642. Pub. country: United States. Language: English.

AB The effect of fenofibrate on plasma cholesteryl ester transfer protein (CETP) activity in relation to the quantitative and qualitative features of apoB- and apoA-I-containing lipoprotein subspecies was investigated in nine patients presenting with combined hyperlipidemia. Fenofibrate (200 mg/d for 8 weeks) induced significant reductions in plasma **cholesterol** (-16%; P < .01), triglyceride (-44%; P < .007), **VLDL cholesterol** (-52%; P = .01), **LDL cholesterol** (-14%; P < .001), and apoB (-15%; P < .009) levels and increased HDL **cholesterol** (19%; P = .0001) and apoA-I (12%; P = .003) levels. An exogenous cholesteryl ester transfer (CET) assay revealed a marked **decrease** (-26%; P < .002) in total plasma CETP-dependent CET activity after fenofibrate treatment. Concomitant with the pronounced reduction in **VLDL** levels (37%; P < .005), the rate of CET from HDL to **VLDL** was significantly reduced by 38% (P = .0001), whereas no modification in the rate of cholesteryl ester exchange between HDL and **LDL** occurred after fenofibrate therapy. Combined hyperlipidemia is characterized by an asymmetrical **LDL** profile in which small, dense **LDL** subspecies (**LDL**-4 and **LDL**-5, d = 1.039 to 1.063 g/mL) predominate. Fenofibrate quantitatively normalized the atherogenic **LDL** profile by reducing levels of dense **LDL** subspecies (-21%) and by inducing an elevation (26%; P < .05) in **LDL** subspecies of intermediate density (**LDL-3**, **d** = 1.029 to 1.039 g/mL), which possess optimal binding affinity for the cellular **LDL** receptor. However, no marked qualitative modifications in the chemical composition or size of **LDL** particles were observed after drug treatment. Interestingly, the HDL **cholesterol** concentration was increased by fenofibrate therapy, whereas no significant change was detected in total plasma HDL mass. In contrast, the HDL subspecies pattern was modified as the result of an increase in the total mass (11.7%) of HDL2a, HDL3a, and HDL3b (d = 1.091 to 1.156 g/mL) at the expense of reductions in the total mass (-23%) of HDL2b (d = 1.063 to 1.091 g/mL) and HDL3c (d = 1.156 to 1.179 g/mL). Such changes are consistent with a drug-induced reduction in CETP activity. In conclusion, the overall mechanism involved in the fenofibrate-induced modulation of the atherogenic dense **LDL** profile in combined hyperlipidemia primarily involves reduction in CET from HDL to **VLDL** together with normalization of the intravascular transformation of **VLDL**

precursors to receptor-active **LDLs** of intermediate density.

L111 ANSWER 3 OF 4 MEDLINE DUPLICATE 2
92114720 Document Number: 92114720. Effects of a resistive training program on lipoprotein--lipid levels in obese women. Manning J M; Dooly-Manning C R; White K; Kampa I; Silas S; Kesselhaut M; Ruoff M. (Movement Science Department, William Paterson College, Wayne, NJ 07470..) MEDICINE AND SCIENCE IN SPORTS AND EXERCISE, (1991 Nov) 23 (11) 1222-6. Journal code: MG8. ISSN: 0195-9131. Pub. country: United States. Language: English.
AB The purpose of this study was to determine the effects of a resistive training program on the time course of changes in strength, body mass index, lipids, lipoproteins, and apolipoproteins in sedentary obese women.
Sixteen sedentary obese women strength trained 3 times . wk-1 for 12 wk performing three sets of six to eight repetitions per set with sets 1 and 2 at 60-70% of one-repetition maximum. During set 3, the subjects used the
greatest weight possible so that failure occurred between six to eight repetitions. Six sedentary obese women served as controls. Blood samples for serum total **cholesterol** (TC), high-density lipoproteins (HDL-C), **low-density lipoproteins** (**LDL**-C), triglycerides (TG), TC/HDL-C ratio, apolipoprotein A-I (apo A-I), and **apolipoprotein B-100** (apo B-100) were obtained pre, and after 4, 8, and 12 wk of training and approximately 3-4 d following the last training session. A **3-d** dietary record was obtained on all subjects pre and post, and subjects were instructed not to alter their diet. The 12 wk of resistive training did not result in a significant change in body weight, BMI, or total kilocalories consumed per day but did show a mean improvement of 58%
in muscular strength (P less than 0.05). The training program did not significantly alter the TC, HDL-C, **LDL**-C, TG, TC/HDL-C ratio, apo A-I, or apo B-100 levels, which suggests that this increase in strength owing to resistive training in the absence of body weight loss did not alter the lipid profiles in these sedentary obese women.

L111 ANSWER 4 OF 4 MEDLINE
90105510 Document Number: 90105510. Structure of human **low**-density lipoprotein subfractions, determined by X-ray small-angle scattering. Baumstark M W; Kreutz W; Berg A; Frey I; Keul J. (Institut fur Biophysik und Strahlenbiologie der Universitat Freiburg im Briesgau, F.R.G..) BIOCHIMICA ET BIOPHYSICA ACTA, (1990 Jan 19) 1037 (1) 48-57. Journal code: A0W. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.
AB The structure of **low**-density lipoprotein (**LDL**) particles from three different density ranges (**LDL**-1: d = 1.006-1.031 g/ml; **LDL-3: d** = 1.034-1.037 g/ml; **LDL**-6: d = 1.044-1.063 g/ml) was determined by X-ray small-angle scattering. By using a theoretical particle model, which accounted for the polydispersity of the samples, we were able to obtain fits of the scattering intensity that were inside the noise interval of the measured intensity. The assumption of deviations from radial symmetry is not supported by our data. This implies a spread-out conformation of the apolipoprotein B (apoB) molecule, which appears to be localized in the
outer surface shell. A globular structure is not consistent with our data.

Furthermore, different models exist concerning the structure of the **cholesterol** ester core below the phase transition temperature. The electron density data suggest an arrangement in which the steroid moieties are localized at average radii of 3.2 and 6.4 nm. Model calculations show that packing problems can only be avoided if approximately half of the acyl chains of each shell are pointing towards the center of the particle, the other half towards the surface. This arrangement of the acyl chains has never been proposed before. The **LDL** particles of different density classes differ mainly with respect to the size of the core but also with respect to the width of the surface shells. Model calculations show that the size of different **LDL** particles can be accurately predicted from the compositional data.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	174.50	191.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.35	-2.35

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